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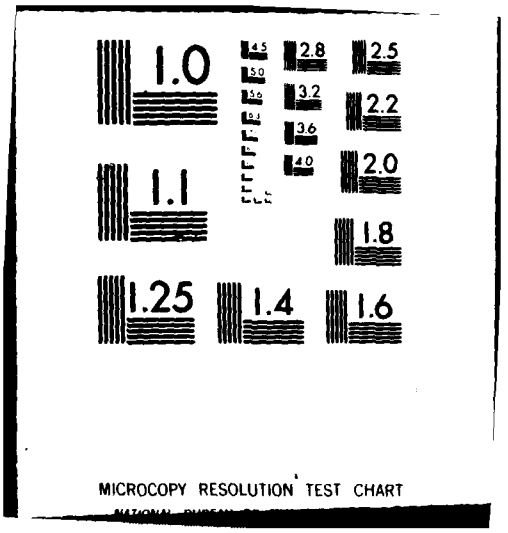
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REPORT NUMBER VII

Chemotherapeutic Studies on Schistosomiasis and Clinical, Epidemiological and Immunological Studies on Malaria in Amazonas, Brazil, Along the Ituxi River.

Final Technical Report
(October 1979 - September 1980)
October 1980

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

The U.S. Army's Anti-Schistosome Drug Development Program, Walter Reed Army Institute of Research, provides selected drugs for testing in mice. The compounds are tested for prophylactic (PMT) or curative (PCT) activity as a primary screen according to pre-established priorities. The program is supported by a Biomphalaria glabrata snail colony capable of providing a daily inventory of 1,000 to 1,500 S. mansoni infected snails. During FY80 a total of 669 bottle number compounds were received from WRAIR and logged in at USAMRU-Brasi-

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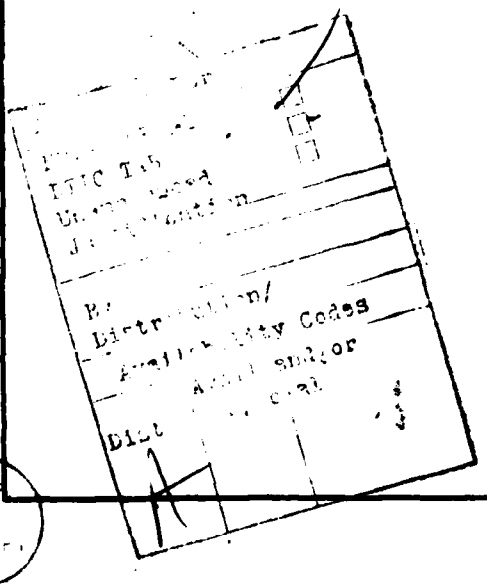
lia laboratory. A total of 1,097 compounds were tested for prophylactic and/or curative activity; of these drugs, 430 were tested in the PMT and 667 were tested in the PCT. In the PMT, 150 compounds were identified as toxic at one or more dosages; and 6 compounds were identified as unconfirmed or confirmed active at one or more dosages. In the PCT, 84 compounds were toxic; and 11 compounds were confirmed or unconfirmed active.

The malaria research program at the University of Brasilia emphasizes investigations of the clinical, epidemiological, immunological and entomological aspects of this disease in a population residing along the Ituxi River in Amazonas, Brazil. The major laboratory and field activities include clinical examination of individual patients for signs of disease, seroepidemiological studies, in vitro chloroquine susceptibility testing of local strains of Plasmodium falciparum, the study of the ecology and population dynamics of malaria vectors, with special emphasis on Anopheles darlingi Root, and investigation of the role of euglossine bees in the removal of DDT from sprayed houses. These studies of malaria, in a region known to be "refractory" to control measures, are designed to collect information which will contribute to an understanding of the mechanisms of continued disease transmission in spite of ongoing eradication efforts. ~~In this respect,~~ extensive investigation were conducted on host seeking behavior of An. darlingi in DDT-sprayed and unsprayed houses and analysis of the results relative to the incidence of malaria in the Amazonas study area. Efforts with the in vitro continuous cultivation of P. falciparum malaria were quite successful. A total of 10 Brasilian strains were isolated, and cryopreserved. Two strains were placed into continuous cultivation for studies of growth characteristics. At least 2 strains show marked to chloroquine in preliminary tests. Extensive seroepidemiology testing was conducted in the Ituxi study area and on the Japurá River in Amazonas. Indirect Fluorescent Antibody Test (IFAT) results for anti-malaria IgM and IgG indicate a very high prevalence of malaria in both areas.



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ANNUAL ACTIVITIES REPORT, FY 1980.

Project: 3M162770A871AH

Work Unit: 009 Antischistosomal Drug Development and Malaria Immunology and Vector Studies.

Investigators: LTC Willis A. Reid, Jr., MAJ Donald R. Roberts, MAJ K. Mills McNeill and Dr. Aluizio R. Prata, MD.

PROBLEM AND OBJECTIVES:

1. Schistosomiasis and malaria continue to be two of the major health problems facing many developing countries in South America, the Carribean, Africa, the Middle East and the Far East, and pose a disease threat to American military personnel stationed in these areas. There is currently no single drug which presents a totally satisfactory treatment for schistosomiasis. The USAMRU-Brasilia antischistosomal drug testing program is oriented to identifying compounds or classes of compounds which elicit prophylactic and curative activity against laboratory Schistosoma mansoni infections.

2. At the same time, major problems are surfacing for the malaria control programs in many malaria endemic areas in South America. These are complex problems involving basic questions on the status of 1) physiological and/or behavioral resistance of vector populations to DDT and 2) drug resistant strains of falciparum malaria. Anopheles darlingi is the major vector species in South America and research along the Ituxi River, in the state of Amazonas, Brazil was conducted to elucidate the parameters of host-seeking and resting behavior of natural populations of this species. An additional objective was to assess the impact of spraying houses with DDT on vector behavior. Concurrently, sero-epidemiological studies were continued to identify disease incidence and prevalence, and in vitro continuous cultivation of malaria parasite strains was instituted for drug resistance analysis and antigen production.

PROGRESS:

1. During FY1980, extensive antischistosomal Primary Curative Testing (PCT) and Primary Prophylactic (Mortality) Testing (PMT) were conducted. In the PMT, test results for 430 different compounds were compiled. Of these 150 were toxic and 6 were active. In the PCT, 667 drugs were tested, of which 84 were toxic and 11 were active. The Secondary Curative Test (SCT) was implemented to further evaluate promising compounds identified in the PCT. Two SCT runs were accomplished, evaluating 5 drugs in more detailed analyses. In all, a total of 36 PCT, PMT and SCT drug test runs were conducted during the year, identifying 17 promising compounds for further evaluation.

2. Malaria vector studies on the behavior of An. darlingi were initiated along the Ituxi River in July, 1978. Systematic collections from human bait and window traps, in combination with mark-release-recapture methods, were conducted to quantify indoor and outdoor activities in both DDT sprayed and unsprayed houses (one house each). Peak host-seeking activity occurred in the peridomiciliary environment at sunset and sunrise. Biting activity within the house was slightly greater during the first half of the night but continued unabated until sunrise, no bimodal activity patterns were found. Peak movements into the house by host-seeking populations and migration out of the house by engorged specimens occurred at sunset and sunrise, respectively. We identified the ceiling as the preferred in-house resting site of both engorged and unengorged specimens of An. darlingi. This determination resulted from repeated observations on in-house distributions of specimens marked with fluorescent powder. Since only the lower part of house ceilings are sprayed (documented by DDT residue analyses), selection of this resting site may reflect an avoidance behavior. Studies on biting activity in a house treated with DDT and in an unsprayed house revealed that populations of An. darlingi were strongly repelled by DDT treated surfaces. Ratios of attack rates per hour for the unsprayed:sprayed houses were 34:1.3 immediately after spraying and 61:2.1 eight weeks post-spraying. Marked populations released inside the DDT treated house left immediately, whereas most specimens released inside the unsprayed house remained in the house until sunrise (6-8 hrs after release). These preliminary results indicate that a significant level of protection is obtained against populations of An. darlingi by spraying houses with DDT. In this respect, the high incidence of malaria in residents along the river probably relate to the human ecological factor of poor house construction and not to any "behavioral resistance" to DDT on the part of the vector.

3. Extensive seroepidemiology testing was conducted in the Ituxi study area and on the Japurá River, also in Amazonas. Indirect Fluorescent Antibody Test (IFAT) results for anti-malaria IgM and IgG indicate very high prevalence of malaria in both areas.

Efforts with the in vitro continuous cultivation of P. falciparum have been very successful. A total of four strains have been cultured in the laboratory, three being new isolates from the state of Amazonas. Initial cultures of Camp Strain Cb1 obtained from the WRAIR were succeeded by successful cultures of strain Ituxi 084 in September 1979, the latter being the first documented Brazilian isolate of P. falciparum to be placed into the system of continuous cultivation. A total of 9 additional strains have been collected and cryopreserved from patients presenting to be treatment facility at the Institute of Tropical Medicine of Manaus. Two of the 9 specimens have been placed into continuous cultivation and excellent growth has been obtained. No cultivation attempts have yet been made with the remaining 7 stabilates. In vitro drug testing has been performed on all 10 strains of P. falciparum

obtained from Amazonas. At least 2 show marked resistance to chloroquine in the preliminary tests and further study of these strains is being performed.

RECOMMENDATIONS:

1. Continue primary screening of antischistosomal curative and prophylactic compounds, especially those of related chemical classes to those compounds already identified as potentially active.

2. Continue secondary curative testing on highly potential compounds.

3. Continue studies to describe the behavioral, morphological and physiological characteristics of selected anopheline species, particularly An. darlingi. Conduct comparative studies in various areas of the Amazon Basin.

4. Assess the impact of house treatment with DDT on malaria vector behavior and population densities in various areas of the Amazon Basin.

5. Colonize An. darlingi for vector competence and behavioral studies under laboratory conditions.

6. Capitalize on the in vitro P. falciparum cultivation capabilities to thoroughly analyze the nature of malaria drug resistance in the Amazon Basin.

7. Interface the malaria immunology capabilities with the malaria vector studies, especially with regard the Recommendations 3 and 5 above.

PRESENTATIONS:

1. McNeill, K.M. 1979. "Técnicas novas para avaliação da resistência da droga em Plasmodium falciparum". Invitational presentation to the "Curso de Extensão sobre Avanços em Medicina Tropical", jointly sponsored by the University of Brasilia and the Ministry of Health, Brazil (Nov 79).

2. Roberts, D.R. 1979. "Resistência dos anofelinos ao DDT". Invitational presentation to the "Curso de Extensão sobre Avanços em Medicina Tropical", jointly sponsored by the University of Brasilia and the Ministry of Health, Brazil (Nov 79).

3. Roberts, D.R. 1979. "Comportamento das Abelhas da Tribo Euglossine atraídas pelo DDT". Invitational presentation to the Reunião Regional de Brasilia da Sociedade Brasileira de Medicina Tropical e Nutrição, Universidade de Brasilia, Brazil (5 Dec 79).

4. Roberts, D.R., J.M. Heller, S.R. Ehrhardt and A.R. Prata. 1979. "DDT como atraente de machos de abelhas Euglossinas, no Brasil".

Invitational presentation to the Academica Brasileira de Ciências, Universidade de São Paulo, São Paulo, Brasil (6 Nov 79).

5. Papers presented at the XVI Congresso da Sociedade Brasileira de Medicina Tropical, 5-8 Feb 1980, Natal, Rio Grande do Norte, Brazil (English translations of original Portuguese titles):

   a. Alecrim, W.D., M.G.C. Alecrim, K.M. McNeill, R. Araujo, A. Viana, J.A. Pires, A. Prata and P. Marsden. "Tropical splenomegaly syndrome in the region of the Ituxi River, Amazonas".

   b. Alecrim, W.D., M.G.C. Alecrim, D.R. Roberts, M.V.F. Guerra, and A.M. Tavares. "Spleen indices and malaria parasite rates in residents along the Ituxi River, Amazonas".

   c. Alecrim, W.D., K.M. McNeill, A.M. Tavares, D.R. Roberts, and J.F. Olimpio. "A serological study of malaria in a population on the Ituxi River, Amazonas".

   d. Alecrim, W.D., D.R. Roberts, K.M. McNeill, H.V. Dourado and A. Prata. "Population migration and malaria control in a malaria endemic area along the Ituxi River".

   e. McNeill, K.M., W.D. Alecrim, A.M. Tavares and D.R. Roberts. "Comparison of malarial antibody activity in filter paper samples and sera by the Indirect Fluorescent Antibody Test".

   f. McNeill, K.M., D.R. Roberts and W.D. Alecrim. "Continuous *in vitro* cultivation of a new strain of Plasmodium falciparum (Ituxi 084)".

   g. Roberts, D.R., W.D. Alecrim, S.R. Erhardt and J.T. Whitlaw "Euplusia purpurata, a bee attracted to DDT on sprayed house walls".

   h. Roberts, D.R., W.D. Alecrim, A.M. Tavares and K.M. McNeill. "Obervations on the behavior of Anopheles darlingi Root in a malaria endemic area of Amazonas, Brazil".

BIBLIOGRAPHY:

1. Marsden, P. and W. Reid. 1980. New Transactions resists predations of the American conckrouch (Periplaneta americana). Submitted for publication to the Transaction of the Royal Society of Tropical Medicine and Hygiene.

2. McNeill, K.M., W.D. Alecrim, A.M. Tavares on D.R. Roberts. 1980. Activity of IgG and IgM in serum and filter paper blood samples in

the Indirect Fluorescent Antibody Test for malaria. Submitted for publication to The American Journal of Tropical Medicine and Hygiene.

3. Peterson, N.E. and R.J. Izor. 1980. Notes on South American weasels. Submitted for publication to the Journal of Mammalogy.

4. Peterson, N.E., D.R. Roberts and C.H. Llewellyn. 1980. A multidisciplinary program of disease surveillance along the Transamazon Highway in Brazil. I. Area ecology. Submitted for publication to the Bulletin of the P.A.H.O.

5. Peterson, N.E. and D.R. Roberts. 1980. A multidisciplinary program of disease surveillance along the Transamazon Highway in Brazil. III. Mammalian surveillance. Submitted for publication to the Bulletin of the P.A.H.O.

6. Phillips, S.M. and W.A. Reid. 1980. Schistosoma mansoni: immune response to normal and irradiated cercariae or soluble stage-specific surface immunogens. International Journal of Nuclear Medicine and Biology, 7:173-186.

7. Phillips, S.M., W.A. Reid, B.L. Doughty and A.G. Bentley. 1980. The immunologic modulation of morbidity in schistosomiasis. Studies in athymic mice and in vitro granuloma formation. American Journal of Tropical Medicine and Hygiene, 29:820-831.

8. Prata, A., W.A. Reid and M.S.L. Cunha. 1980. Tratamento da Giardiose com Tinidazol. Submitted for publication to the Revista da Sociedade Brasileira de Medicina Tropical.

9. Roberts, D.R. and B.P. Hsi. 1979. An index of species abundance for use with mosquito surveillance data. Environmental Entomology 8:1007-1013.

10. Roberts, D.R. and J.E. Scanlon. 1979. An evaluation of morphological characters for separating females of Aedes (Ochlerotatus) atlanticus Dyar and Knab and Aedes (Ochlerotatus) tormentor Dyar and Knab (Diptera: Culicidae). Mosquito Systematic. 11:203-208.

11. Roberts, D.R., J.M. Heller, W.D. Alecrim, S.R. Ehrhardt and A. Prata. 1980. DDT- an attractant to male euglossine bees in Brazil. Submitted for publication to Science.

12. Roberts, D.R., A.L. Hoch and N.E. Peterson. 1980. A multidisciplinary program of infectious disease surveillance along the Transamazon Highway in Brazil. IV. Entomological surveillance. Submitted for publication to the Bulletin of the P.A.H.O.

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